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| 10/550,295 | 02/23/2006 | Marie-Anne Petit | 0508-1140 | 2042 |
| 465 7590 09/17/2008 YOUNG & THOMPSON 209 Madison Street Suite 500 ALEXANDRIA, VA 22314 | | | EXAMINER BOESEN, AGNIESZKA | |
| | | | ART UNIT 1648 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/550,295

Applicant(s)

PETIT ET AL.

Examiner

AGNIESZKA BOESEN

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1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 77 and 78 is/are allowed.
- 6) ☒ Claim(s) 69-74 and 79-81 is/are rejected.
- 7) ☒ Claim(s) 75 and 76 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S5108)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The Amendment filed June 18, 2008 in response to the Office Action of March 18, 2008 is acknowledged and has been entered. Claims 35-68 have been canceled. New claims 69-81 have been added and are under examination in this Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Rejection of claims 35-43 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter **is moot** because Applicant canceled the claims.

However the same rejection is made to new claims in view of Applicants amendment

Claims 69-74 and 79-81 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims are drawn to a conformational antibody capable of specifically binding to the natural HCV viral envelope. Claims are rejected because the claims do not define over the naturally generated anti-HCV viral envelope antibodies as they are found in nature. For example the antibodies generated in a human infected with HCV read on the claimed antibodies. The recitation of "conformational" antibody is interpreted to refer to a conformational epitope antigen to which an antibody typically binds. A conformational anti-HCV envelope antibody would be typically generated in an HCV infected subject. Thus the recitation of "conformational" antibody does not define the present antibodies as different from those found in nature. Therefore the claims are rejected as being drawn to non-statutory subject matter.

Response to Applicant's arguments

Applicant's arguments have been fully considered but fail to persuade. Applicants argue that since there is no indication in the art of antibodies binding the three regions of E1 297-306, E2 480-494, and E2 613-621, the conformational antibodies of the present invention are clearly human made invention that gives these materials new properties and qualities.

In response to Applicant's arguments it is the Office position that the claimed antibodies are products of nature as evidenced by Petit et al. (Journal of Biochemical Chemistry, Nov. 2003, Vol. 278, p. 44385-44392, see Abstract) and Fount et al. (WO 02/057314 A2). As discussed below Fount discloses antibodies binding E1 and E2 isolated from patients infected with HCV. Thus because the claimed antibodies read on the antibodies naturally made in humans infected with HCV the rejection is maintained.

Claim Rejections - 35 USC § 112

Rejection of claims 44-47 and 51 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is moot** because Applicant canceled the claims.

New claims 75-78 are not rejected because Applicant submitted the biological deposit information for CNCM I-2983 and CNCM I-2982.

Claim Rejections - 35 USC § 102

Rejection of claims 35-40, and 43 under 35 U.S.C. 102(b) as being anticipated by Cocquerel et al. (Journal of Virology, January 2003, Vol. 77, p. 1604-1609 in IDS of 9/21/2005) **is moot** because Applicant canceled the claims.

Rejection of claims 35-41, 43, and 48 under 35 U.S.C. 102(b) as being anticipated by Fount et al. (WO 02/057314 A2) **is moot** because Applicant canceled the claims.

Rejection of claims 64 and 65 under 35 U.S.C. 102(b) as being anticipated by Lechmann et al. (Hepatology, 2001, Vol. 34, p. 417-423) **is moot** because Applicant canceled the claims.

New Rejections in view of Applicant's amendment

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 69-74 and 79-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Lechmann et al. (Hepatology, 2001, Vol. 34, p. 417-423).

Claims are drawn to a conformational monoclonal antibody capable of specifically binding to the natural HCV viral envelope epitopes: E1 297-306, E2 480-494, and E2 613-621. The antibody is capable of precipitating the HCV E1E2 complex under of a non covalent form. Claims are drawn to an antibody that binds to the natural HCV E1 protein. Claims are drawn to a process for preparing a monoclonal antibody capable of binding to natural HCV viral envelope comprising immunizing an animal with a composition of HCV viral particles and selecting monoclonal antibodies that bind to the HCV viral particles.

Lechmann et al. disclose methods for preparing monoclonal conformational antibodies in mice; comprising immunizing an animal with a composition of HCV virus like particles comprising E1 and E2 envelope glycoprotein and selecting antibodies that bind to the E1/E2 of

the HCV viral particles (see Materials and Methods). Lechmann's composition comprises a pharmaceutically acceptable carrier such as an adjuvant (see page 418). Lechmann et al. specifically disclose that after the fifth immunization of mice with HCV virus like particles the anti-E1/E2 antibodies were detected with titers ranging from 200 to 800 (see under Results on page 418).

It is the position of the Office that the anti-E1/E2 antibodies disclosed by Lechman bind the HCV viral envelope epitopes: E1 297-306, E2 480-494, and E2 613-621, because Lechmann's antibodies were made by the same process as the antibodies of the present invention and because Lechmann's HCV virus like particles contain E1 and E2 comprising the present SEQ ID NO: 1, 2 and 3. Applicant's specification and the claims disclose generation of conformational antibodies comprising immunizing mice with HCV virus like particles (see Example 2 and claims 81 and 81. Thus because the antibodies disclosed by Lechmann were made by the same process as the antibodies of the present invention, it is the position of the Office that Lechmann's antibodies bind HCV viral envelope epitopes: E1 297-306, E2 480-494, and E2 613-621. It is noted that the recitation of "an epitope constituted of" is interpreted as an open claim language with regard to the sequences SEQ ID NO: 1, 2 and 3. Since Lechmann's antibodies bind E1/E2 complex, Lechmann's antibodies should be capable of precipitating the E1/E2 complex. Thus by this disclosure Lechmann et al. anticipate the present claims.

The Office shifts the burden on Applicant to prove that antibodies of the present invention are distinct from the antibodies disclosed by Lechmann (see MPEP 2112.1).

MPEP 2112.01 Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical

processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)

Claims 69-74 and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Foug et al. (WO 02/057314 A2).

Claims are drawn to a conformational monoclonal antibody capable of specifically binding to the natural HCV viral envelope and a pharmaceutical composition comprising the anti-HCV antibodies and a pharmaceutically acceptable vehicle. The antibody is capable of precipitating the HCV E1E2 complex of a non covalent form. Claims are drawn to an antibody that binds to the natural HCV E1 protein. The conformational antibody binds an epitope constituted of at least one of epitopes: E1 (aa 297-206), E2 (aa 480-494) and E2 (aa 613-621).

Foug et al. disclose a monoclonal antibody binding a conformational epitope of E1 and E2 protein of HCV (see claims 2 and 3). Foug et al. disclose a monoclonal antibody binding conformational epitopes spanning the amino acids 470 through 644 of E2 protein (see claims 9 and 10). The epitope disclosed by Foug comprises the present epitopes E2 (aa 480-494) and E2 (aa 613-621). Thus Foug’s antibody binds the E2 (aa 480-494) and E2 (aa 613-621) epitopes of

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the present invention. Sequence search analysis of SEQ ID NO: 3 recited in the present claims reveals that the amino acids 613-621 of the E2 (SEQ ID NO: 3) are identical with the amino acids of the E2 epitope disclosed in the prior art (see sequence comparison below, note that the Query represents amino acids 613-621 of the E2 SEQ ID NO: 3, and the Db represents SEQ ID NO: 192AA of Fountg).

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QY      XXXXXXXXXXXXXXXXXXXXXYRLWHYPCTXXXXXXXXXXXXXXXXXXXXXXXXX
        ::::::::::::::::::::||| ||| ||| ::::::::::::::::::::
Db      TYTKCGSGPWLTPRCIVDYPYRLWHYPCTVNFTIFKVRMYVVGMEHRLN

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Fountg et al. disclose a pharmaceutical composition comprising the antibody specifically binding to the natural HCV viral envelope and a pharmaceutically acceptable vehicle (see claim 29).

It is noted that Fountg's antibodies were isolated from humans infected with HCV (see Examples 1-3 and 5). Fountg does not disclose a specific epitope of E1 to which his antibody binds. However it is the position of the Office that Fountg's antibody binds epitopes: E1 (aa 297-206), E2 (aa 480-494) and E2 (aa 613-621). The Office shifts the burden on Applicant to prove that the antibodies of the present invention are distinct from the antibodies in the prior art.

It is noted that the functional limitations recited in the present claims with regard to the antibody being capable of precipitating the HCV E1E2 complex and neutralizing the HCV infections in patients, the limitations are considered to be an inherent property of the antibodies disclosed in the prior art. Because Fountg's antibodies bind epitopes within the E1 and E2 protein, these antibodies are expected to precipitate the E1E2 complex and to neutralize the HCV infections in patients. Thus Fountg et al. anticipate the present claims.

Claim Objections

Claims 75 and 76 are objected to as being dependent from rejected claims. The claims would be allowable if rewritten in independent form.

Conclusion

Claims 69-74 and 79-81 are rejected.

Claims 77 and 78 are allowable.

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Thus, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648